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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	27

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/341,641	Schmidt et al.
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- *Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.*
- *If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.*
- *If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.*
- *Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).*
- *Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).*

Status

1) ☒ *Responsive to communication(s) filed on Oct 21, 2002 .*

2a) ☒ *This action is* **FINAL.** 2b) ☐ *This action is non-final.*

3) ☐ *Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.*

Disposition of Claims

4) ☒ *Claim(s) 21-39 and 41-43 is/are pending in the application.*

4a) *Of the above, claim(s) _____ is/are withdrawn from consideration.*

5) ☐ *Claim(s) _____ is/are allowed.*

6) ☒ *Claim(s) 21-39 and 41-43 is/are rejected.*

7) ☐ *Claim(s) _____ is/are objected to.*

8) ☐ *Claims _____ are subject to restriction and/or election requirement.*

Application Papers

9) ☐ *The specification is objected to by the Examiner.*

10) ☐ *The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.*

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ *The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.*

If approved, corrected drawings are required in reply to this Office action.

12) ☐ *The oath or declaration is objected to by the Examiner.*

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ *Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).*

a) ☐ *All* b) ☐ *Some** c) ☐ *None of:*

1. ☐ *Certified copies of the priority documents have been received.*
2. ☐ *Certified copies of the priority documents have been received in Application No. _____ .*
3. ☐ *Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).*

**See the attached detailed Office action for a list of the certified copies not received.*

14) ☐ *Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).*

a) ☐ *The translation of the foreign language provisional application has been received.*

15) ☐ *Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.*

Attachment(s)

1) ☐ *Notice of References Cited (PTO-892)*
2) ☐ *Notice of Draftsperson's Patent Drawing Review (PTO-948)*
3) ☐ *Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____*
4) ☐ *Interview Summary (PTO-413) Paper No(s). _____*
5) ☐ *Notice of Informal Patent Application (PTO-152)*
6) ☐ *Other:*

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 21-32 are rejected under 35 U.S.C. 102 (b) as anticipated by Southern et al. (PCT International Publication Number: WO 95/04160) (February 9, 1995).

This rejection is based on the assumption that "same reaction zone" means common sequences on plurality of DNA templates where hybridization reaction takes place.

Southern et al. teaches a method for sequencing DNA (Abstract with Figure), which comprises:

(a) obtaining a target DNA population comprising a plurality of single-stranded DNAs to be sequenced, each of which is present in a unique amount in the same reaction zone and bears a primer to provide a double-stranded portion of the DNA for ligation thereto(Figure 5 and Example 16 b, lines 1-12 and Claims 16 a and 16 b);

(b) contacting the DNA population with an array of hybridization probes, each probe comprising a label cleavably attached to a known base sequence of predetermined length, the array containing all possible base sequences of that predetermined length and the base sequence being incapable of ligation to each other, wherein the contacting is carried out in the presence of

ligase under conditions to ligate to the double-stranded portion of each DNA the probe bearing the base sequence complementary to the single-stranded DNA adjacent the double-stranded portion thereby to form an extended double-stranded portion which is incapable of ligation to further probes (Figures 4 and 5 and Claims 16 a to 16 d and Claims 20 a to 20 d);

c) removing all unligated probes (Claims 16 e and 20 e); followed by the steps of :

(d) cleaving the ligated probes to release each label (Figures 3a, 3b and 4, and Page 16, lines 5-18 and Example 18);

(e) recording the quantity of each label (Example 19, Figures 3b, 4 and 5 and claims 16 f and 20 f); and

(f) activating the extended double-stranded portion to enable ligation thereto (Page 16, lines 15-18, Figures 4 and 5);

(g) steps (b) to (f) are repeated in a cycle for a sufficient number of times to determine the sequence of each single-stranded DNA by determining the sequence of release of each label (Figure 4 and page 16, lines 19-26 and claim 17).

Southern et al. teaches a method wherein the array comprises a plurality of sub-arrays which together contains all possible base sequnces (Page 17, line 1 to page 18, line 5 and page 19, line 26 to page 21, lines 23 and claim 20).

Southern et al. teaches a method wherein the initial DNA sample is cut into fragments, each having a sticky end of known length and unknown sequence, which fragments are sorted into subpopulations according to their sticky end sequence (Example 16 b).

Southern et al. teaches a method wherein each single-stranded DNA is immobilized at one end (Figures 4 and 5).

Southern et al. teaches a method wherein the label of each probe comprises a mass label, and the quantity of each label is recorded using mass spectrometry after release of the label (Example 19).

Southern et al. teaches a method wherein the known base sequence is blocked at its 3' OH (Figure 4, step 1).

Southern et al. teaches a method wherein the step of cleaving the ligated probes to release each label unblocks the 3' -OH of the extended double-stranded portion (Figure 4, step 2).

Southern et al. teaches a method wherein the label of each probe is cleavably attached to the 3'-OH of the base sequence (Figure 4).

Southern et al. teaches a method wherein the base sequence of each probe is unphosphorylated at both 3' and 5' ends and comprises phosphorylating the 5'-OH of the extended double-stranded position (Figure 4, steps 3 and 4).

Southern et al. teaches a method wherein the predetermined length of the base sequence is from 2 to 6 (Page 2, lines 2-8).

3. Claims 21-25 and 27-32 are rejected under 35 U.S.C. 102 (a) as anticipated by Macevicz et al. (PCT International Publication Number: WO 96/33205) (October 24, 1996).

Macevicz et al. teaches a method for sequencing DNA (Abstract with Figure), which comprises:

(a) obtaining a target DNA population comprising a plurality of single-stranded DNAs to be sequenced, each of which is present in a unique amount in the same reaction zone and bears a primer to provide a double-stranded portion of the DNA for ligation thereto(Figure 1 and page 10, lines 16 to page 11, lines 23);

(b) contacting the DNA population with an array of hybridization probes, each probe comprising a label cleavably attached to a known base sequence of predetermined length, the array containing all possible base sequences of that predetermined length and the base sequence being incapable of ligation to each other, wherein the contacting is carried out in the presence of ligase under conditions to ligate to the double-stranded portion of each DNA the probe bearing the base sequence complementary to the single-stranded DNA adjacent the double-stranded portion thereby to form an extended double-stranded portion which is incapable of ligation to further probes (Figures 1-4 and Claim 13);

c) removing all unligated probes (Claim 13); followed by the steps of :

(d) cleaving the ligated probes to release each label (Figures 1-4);

(e) recording the quantity of each label (Example 1, page 21, lines 19-27); and

(f) activating the extended double-stranded portion to enable ligation thereto (Figures 1-4 and Example 1, page 21, last paragraph);

(g) steps (b) to (f) are repeated in a cycle for a sufficient number of times to determine the sequence of each single-stranded DNA by determining the sequence of release of each label (Figures 1-4 and Example 1, page 21, last paragraph).

Macevicz et al. teaches a method wherein the array comprises a plurality of sub-arrays which together contains all possible base sequnces (Example 1).

Macevicz et al. teaches a method wherein the initial DNA sample is cut into fragments, each having a sticky end of known length and unknown sequence, which fragments are sorted into subpopulations according to their sticky end sequence (page 5, line 25 to page 6, line 18).

Macevicz et al. teaches a method wherein each single-stranded DNA is immobilized at one end (Figures 1-4).

Macevicz et al. teaches a method wherein the known base sequence is blocked at its 3' OH (Figure 4, step 2).

Macevicz et al. teaches a method wherein the step of cleaving the ligated probes to release each label unblocks the 3' -OH of the extended double-stranded portion (Figure 4, step 3).

Macevicz et al. teaches a method wherein the label of each probe is cleavably attached to the 3'-OH of the base sequence (Figure 4, steps 4 and 5).

Macevicz et al. teaches a method wherein the base sequence of each probe is unphosphorylated at both 3' and 5' ends and comprises phosphorylating the 5'-OH of the extended double-stranded position (Figures 2 and 3b).

Macevicz et al. teaches a method wherein the predetermined length of the base sequence is from 2 to 6 (Page 7, lines 7-20).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 21-39 and 41-43 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Southern et al. (PCT International Publication Number: WO 95/04160) (February 9, 1995) in view of Stratagene Catalog (1988, page 39).

Southern et al teaches the method of claims of 21-32 including array of hybridization probes comprising mass labels as described above.

Southern et al does not teach the motivation to combine all the reagents for identifying a base at a target position in a single-stranded sample DNA sequence in the form of a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine all the reagents e.g., array of hybridization probes comprising mass labels etc. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control". (page 39, column 1).

Response to Arguments

6. Applicant's arguments filed on October 21, 2002 have been fully considered but they are not persuasive..

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., (I) the invention provides a method for analyzing heterogeneous sib-populations of nucleic acids

without spatially resolving them, (ii) all the tags to be detected simultaneously, and (iii) hybridization and ligation takes place simultaneously) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant has argued that heterogeneous population of single stranded DNAs are not disclosed either by Southern or Macevicz references. This argument is not persuasive in view of the fact that a long chain of single stranded DNA can be considered as several different small single stranded DNA(heterogeneous DNAs) joined together. Moreover Southern et al clearly teaches heterogeneous population as Southern et al recites, "An advantage of this approach is that very large numbers of DNA sequences can be analyzed together (Page 18, lines 3-5)". Applicant also argues that Souther reference does not teach probes "incapable of ligation to each other". This argument is not persuasive. Figure 4 clearly and inherently teaches probes with codes at one end which is incapable of ligation to each other. Applicant also argues that Southern does not teach ligation and hybridization simultaneously. This argument is not persuasive. Example 16b clearly and inherently teaches ligation and hybridization simultaneously (Page 44, lines 32-35).

Applicant argues that neither of the references teaches the determination of the quantity of each label of the claimed invention. Applicant argues that the word " determination of the quantity of each label" was not found in any reference. Applicant argues that because Southern and Macevicz has a preferred embodiment of mass spectrometric determination and

fluorescence determination respectively, Southern and Macevicz are limited to the preferred embodiment. This argument is not persuasive. As MPEP 2123 states "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi,169 USPQ 423 (CCPA 1971)." MPEP 2123 also states " A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989)." It is clear that simply because Southern and Macevicz have a preferred embodiment, this embodiment does not prevent the references from suggesting broader embodiments in the disclosure and that this does not constitute a teaching away. Although Southern and Macevicz references use mass spectrometric and fluorescence determination respectively, the property of determination of quantity of each label is inherently present in this chemically and structurally identical molecule. For example, Southern et al. teaches, "In both cases the peaks are absent from the oligonucleotides which have no tag (Example 19, page 46, lines 25-26)". Southern et al clearly teaches identification and quantification inherently by mass spectrometry of different tags attached to different analytes (Example 19). Moreover, MPEP 2111 states, "Claims must be given their broadest reasonable interpretation. During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than it is justified. *In re*

Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969)". In this case, identification by mass spectrometry and fluorescence of Southern and Macevicz can be considered as quantification of each label.

Therefore, all the 102 rejections made in the first office action are hereby properly maintained.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

November 6, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600